AD_________________

AWARD NUMBER: W81XWH-04-1-0481

TITLE: High Resolution X-ray Phase Contrast Imaging With Acoustic Tissue-Selective Contrast Enhancement

PRINCIPAL INVESTIGATOR: Gerald J. Diebold, Ph.D.

CONTRACTING ORGANIZATION: Brown University
Providence, Rhode Island 02912

REPORT DATE: June 2006

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
01-06-2006	Annual	1 Jun 2005 – 31 May 2006

4. TITLE AND SUBTITLE

High Resolution X-ray Phase Contrast Imaging With Acoustic Tissue-Selective Contrast Enhancement

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-04-1-0481

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Gerald J. Diebold, Ph.D.

E-Mail: Gerald_Diebold@Brown.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Brown University
Providence, Rhode Island 02912

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

We show that ultrasound can be used for contrast enhancement in high-resolution x-ray imaging of tissue and soft materials. Interfacial features of objects are highlighted as a result of both the displacement introduced by the ultrasound and the inherent sensitivity of x-ray phase contrast imaging to density variations. Experimental results are reported for tumor phantoms. The method produces a directional image that is equivalent to the first space derivative of the phase contrast image along the propagation coordinate of the ultrasound.

15. SUBJECT TERMS
X-ray, ultrasound, phase contrast, imaging, elastography

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
U	U	U	UU	9	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

Introduction

Acoustically Modulated X-ray Phase Contrast Imaging

The method of modifying a phase contrast image using acoustic radiation pressure [21,22] consists of two steps: first, an x-ray image is made with a sound beam directed into a body to displace an object through acoustic radiation force and the image stored in a computer, second, another x-ray image is of the object is taken, this time without the presence of the sound beam. Both images are recorded in the compute and then subtracted pixel by pixel to give a subtracted phase contrast image, the component of the image from absorption contrast being largely eliminated, leaving a nearly pure phase contrast image, inherently background and flatfield corrected. Figure 1 gives a diagram of the experimental apparatus.

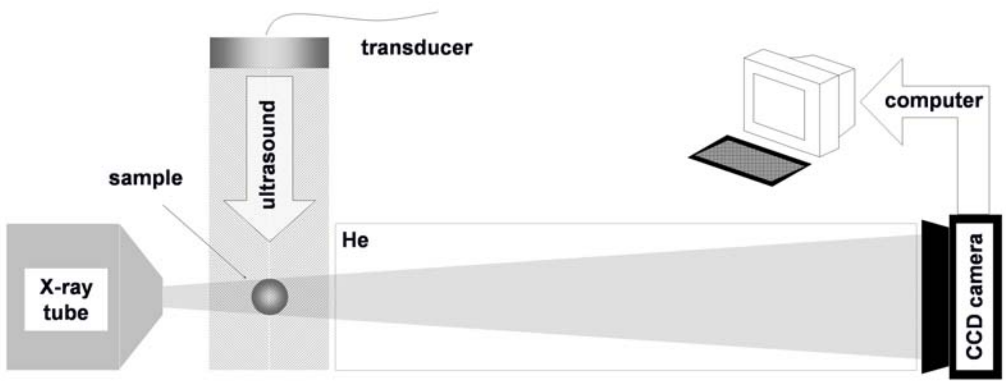

Figure 1 : Diagram of the experimental apparatus. X-radiation generated by a microfocus tube penetrates a sample and is detected by a CCD camera that views a scintillation plate. The CCD camera is read by the computer which stores the images and performs the subtractions.

Body

Figure 2 shows the results of a set of experiments involving a simulated breast. The phantom (purchased from CIR, Inc.) was designed to simulate both the physical density and attenuation characteristics of breast tissue under x-ray and ultrasound exposure. The interior of the phantom contains two types of masses; one with the density and elasticity of malignant tumors and the other with the density of fluid-filled cysts. The results show that the “tumors” respond to the applied 1.14 MHz, 300W sound field whereas the “cysts” do not. This is a significant development since it would give clinicians the ability to differentiate common and benign cysts from malignant tumors.

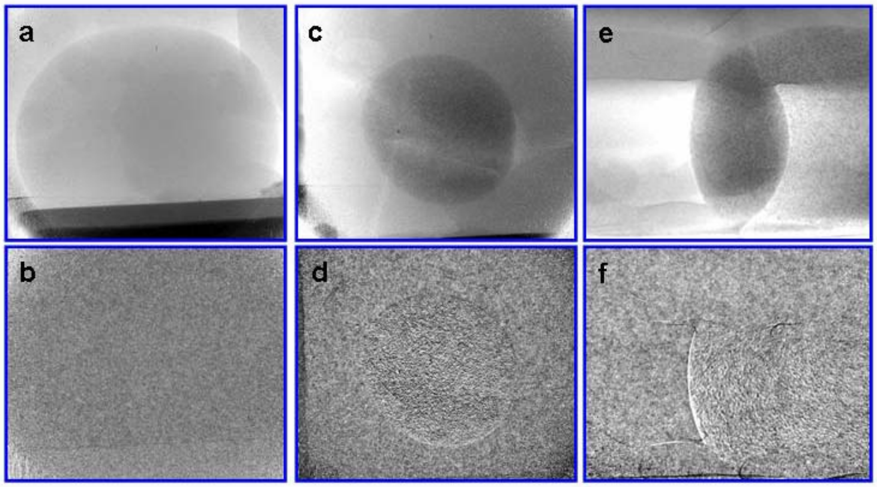

Figure 2 (a) Phase contrast image of a phantom cystic mass; (b) subtracted phase contrast image of (a); (c) phase contrast image of a phantom malignant tumor; (d) subtracted phase contrast image of (c); (e) phase contrast image of the intersection of the cystic and malignant masses placed to the left and right of center, respectively. Note that the image of the cyst is not visible after subtraction, yet the image of the tumor remains.

Figure 3 shows the results of an experiment designed to test the ability of the ultrasonic beam to penetrate biological tissue and produce differential motion. A Teflon bead was embedded in the center of a piece chicken muscle and exposed to a 1.14 MHz, 300W ultrasonic beam. The Teflon bead was clearly moved despite being tightly embedded in the tissue. The additional objects seen in the image are fat bubbles and would not be expected to be a source of background in breast tissue.

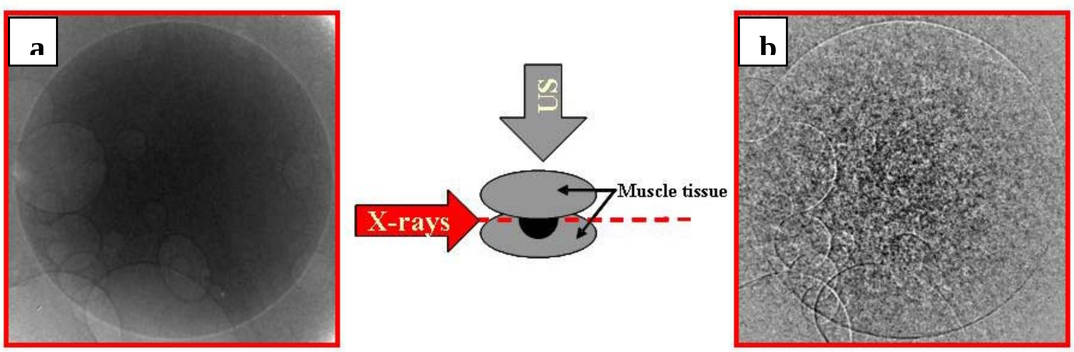

Figure 3. (a) Phase contrast image of a Teflon bead embedded in muscle tissue; (b) subtracted image of (a). The additional round objects are fat bubbles.

We have also tested the ability of our technique to manipulate mouse skin tumors given to us by our collaborators at Brown University Medical School. Figure 4 shows the results of an experiment with one of the skin tumors; the image on the left is a phase contrast image of the tumor and surrounding skin, the image on the right shows the subtracted image. Note that the tumor appearance is enhanced while the background is essentially flat.

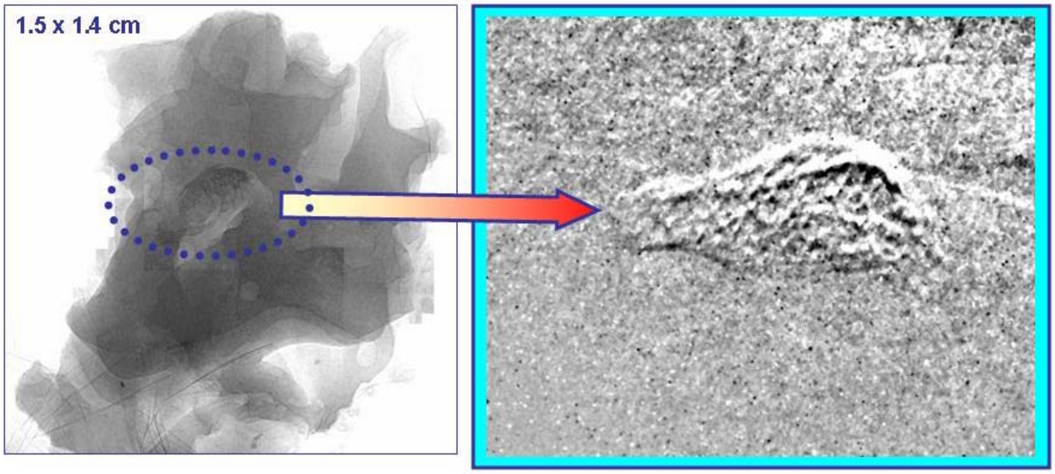

Figure 4. The left-hand image shows the x-ray phase contrast image of the skin tumor; the right-hand image shows the ultrasound-enhanced subtracted image of the tumor.

We have also explored the response of ultrasonic contrast agents to the combination of both x-rays and ultrasonic pressure in an effort to gauge their potential for use as x-ray contrast agents. The bubbles shown in Figure 5 are gas-filled protein shells dispersed in an agarose matrix. The images show that these bubbles respond to the ultrasonic field differently than do solid or fluid-filled spheres. Instead of being pushed by the acoustic pressure, they expand and contract radially.

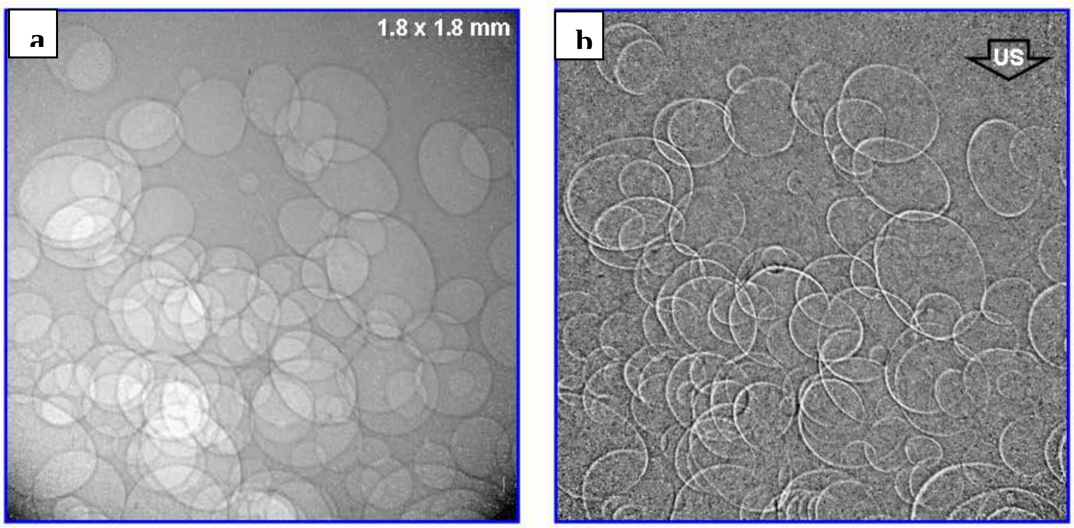

Figure 5 (a) Phase contrast image of gas-filled protein bubbles in an agarose matrix (b) subtracted image showing radial contraction and expansion in response to the applied ultrasonic field.

Reportable Outcomes

"Acoustically Modulated X-Ray Phase Contrast and Vibration Potential Imaging" with a. C. Beverideg, C. J. Bailat, T. J. Hamilton, S. Wang, C. Rose-Petruck, and V. E. Gusev (Proc. SPIE 2005) **selected as the best conference paper**

C. J. Bailat, T. J. Hamilton, C. Rose-Petruck, G. J. Diebold, Acoustic radiation pressure: a phase contrast agent for x-ray phase contrast imaging, Appl. Phys. Lett., Vol. 85 No. 19, Nov. 2004, 4517-4519.

"Ultrasonically modulated x-ray phase contrast and vibration potential imaging methods", with Theron J. Hamilton, Guohua Cao, Shougang Wang, Claude J. Bailat, Cuong K. Nguyen, Shengqiong Li, Stephan Gehring, Jack Wands, Vitalyi Gusev, Christoph Rose-Petruck, Proc. SPIE Vol. 6086, Photons Plus Ultrasound: Imaging and Sensing (2006)

"Ultrasonically Modulated X-ray Phase Contrast Imaging", with Theron J. Hamilton, Guohua Cao, Claude J. Bailat, Jack Wands, Stephan Gehring, Christoph Rose-Petruck (2006)

"X-ray Phase Contrast Imaging: Transmission Functions Separable in Cartesian Coordinates", with Guohua Cao, Theron Hamilton, and Christoph Rose-Petruck (submitted for publication)

"X-ray Phase Contrast Imaging: Experiments and Calculations with Objects having Transmission Functions Separable in Cartesian Coordinates", with Theron J. Hamilton, Guohua Cao, Phillip Wintermeyer, Jack Wands, and Cristoph Rose-Petruck (submitted for publication)

Conclusions

We have completed all the necessary construction of experimental apparatus and proven the concept of ultrasonically modified x-ray phase contrast imaging. We have shown the method has the ability to select objects within a body for imaging and have demonstrated the feasibility of the technique with phantoms and biological samples.

References

1. Born, M. & Wolf, E. *Principles of Optics* (ed. Press, P.) (Pergamon Press, Oxford, England, 1980).
2. Cowley, J. M. (ed.) *Electron Diffraction* (Kluwer Academic Publishers, Dordrecht, 1991).
3. Cowley, J. M. *Diffraction Physics* (North Holland Physics Publishing, a division of Elsevier Science Publishers B.V., Amsterdam, 1984).
4. A Snigirev, I. S., V Kohn, S Kuznetsov, I Schelokov. On The Possibility of X-ray Phase Contrast Microimaging by Coherent High-energy Synchrotron Radiation. *Rev. Sci. Instr.* **66**, 5486 (1995).
5. Fulvia Arfelli, V. B., Alberto Bravin, Giovanni Cantatore, Edoardo Castelli et al. Mammography with Synchrotron Radiation: Phase Detection Techniques. *Radiology* **215**, 286-293 (2000).
6. Momose, A. Demonstration of phase-contrast x-ray computed tomography using an x-ray interferometer. *Nuclear Instruments & Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors, and Associated Equipment* **352**, 622-8 (1995).
7. Pogany, A., Gao, D. & Wilkins, S. W. Contrast and resolution in imaging with microfocus x-ray source. *Rev. Sci. Instr.* **68**, 2774 (1997).
8. Krol, A. et al. Laser-based microfocused x-ray source for mammography: Feasibility study. *Medical Physics* **24**, 725-732 (1997).
9. Krol, A., Kieffer, J. C. & Forster, E. Laser-driven x-ray source for diagnostic radiology. *Proceedings of SPIE-The International Society for Optical Engineering* **3157**, 156-163 (1997).
10. Beckmann, F., Bonse, U., Busch, F. & Gunnewig, O. X-ray microtomography (microCT) using phase contrast for the investigation of organic matter. *Journal of Computer Assisted Tomography* **21**, 539-53 (1997).
11. Westervelt, P. The Theory of steady Forces Caused by Sound Waves. *J. Acoust. Soc. Am.* **23**, 312 (1951).
12. Morse, P. M. *Vibration and Sound* (ed. Physics, A. I. o.) (Acoustical Society of America, 1981).
13. Muthupillai, R. et al. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science (Washington, D. C.)* **269**, 1854-7 (1995).
14. Gao, L., Parker, K. J., Lerner, R. M. & Levinson, S. F. Imaging of the elastic properties of tissue--a review. *Ultrasound in Medicine and Biology* **22**, 959-77 (1996).
15. Fatemi, M. & Greenleaf, J. F. Ultrasound-stimulated vibro-acoustic spectrography. *Science* **280**, 82-5 (1998).
16. Nightingale, K., Nightingale, R., Palmeri, M. & Trahey, G. in *IEEE Ultrasonics Symp* 1319 (1999).
17. Sarvazyan, A. P. Shear Wave Elasticity Imaging: A New Ultrasonic Technology of Medical Diagnostics. *Ultrasound in Medicine and Biology* **24**, 1419 (1998).
18. McAleavey, S. A. Estimates of Echo Correlation and Measurement Bias in Acoustic Radiation Force Impulse Imaging. *IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control* **50**, 631 (2003).

19. Nightingale, K., Stutz, D., Bentley, R. & Trahey, G. in *IEEE Symp* 525 (2002).
20. King, L. V. On the Acoustic Radiation Pressure on Spheres. *Proceedings of the Royal Society of London, Series A, Mathematical and Physical Sciences* **147**, 212-240 (1934).
21. C. J. Bailat, T. Hamilton, Rose-Petruck, C. & Diebold, G. J. Acoustic radiation pressure: a phase contrast agent for x-ray phase contrast imaging. *Appl. Phys. Lett.* **85**, 4517-4519 (2004).
22. T. Hamilton, C. J. Bailat, Rose-Petruck, C. & Diebold, G. J. Acoustically Modulated X-ray Phase Contrast Imaging. *Phys Med Biol* **49**, 4985-4996 (2004).
23. Wilkins, S. W., Gureyev, T. E., Gao, D., Pogany, A. & Stevenson, A. W. Phase-contrast imaging using polychromatic hard x-rays. *Nature* **384**, 335-338 (1996).
24. Radon, J. Über die Bestimmung von Funktionen durch Integralwerte längs gewisser Mannigfaltigkeiten, Berichte Sächsische Akademie der Wissenschaften. *Math.-Phys. Kl.* **69**, 262-267 (1917).